

**External Peer Review of the FDA/CFSAN Draft Qualitative Risk Assessment: Risk of Activity/Food Combinations for Activities (Outside the Farm Definition) Conducted in a Facility Co-Located on a Farm**

**Peer Review Report**

**Office of Food Safety  
Center for Food Safety and Applied Nutrition  
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## **I. Introduction**

The Food and Drug Administration (FDA) has conducted a qualitative risk assessment (RA) related to manufacturing, processing, packing and holding activities for human food when such activities are conducted on farms. This RA was conducted to satisfy requirements of the FDA Food Safety Modernization Act (FSMA). Its requirements were to conduct a science-based risk analysis and to consider the results of that analysis in determining whether to exempt small or very small businesses that are engaged only in specific types of on-farm manufacturing, processing, packing, or holding activities, that FDA determines to be low risk involving specific foods FDA determines to be low risk from the requirements of Sections 418 and 421 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), or whether to modify such requirements for such facilities. The purpose of the RA is to provide a science-based assessment of on-farm activity/food combinations to determine which are considered low risk.

Under the statutory and regulatory framework applicable to farms and to food facilities co-located on farms, a specific activity (such as washing fruits and vegetables) may have a different classification within the classes of manufacturing, processing, packing and holding (with consequences for what regulations apply to the activity) based on whether the food being operated upon is a raw agricultural commodity (RAC) or a processed food. It also depends on whether a RAC was grown or raised on the farm performing the activity or a farm under the same ownership. Therefore FDA arranged the results of the RA in groupings shaped by these factors and the resulting activity classifications:

- Group 1: Low-risk packing and holding activities that might be conducted on a farm on food not grown, raised, or consumed on that farm or another farm under the same ownership;
- Group 2: Low-risk manufacturing and processing activities that might be conducted on a farm on the farm's own RACs for distribution into commerce; and
- Group 3: Low-risk manufacturing and processing activities that might be conducted on a farm on food other than the farm's own RACs for distribution into commerce.

## **II. Peer Review Charge and Questions**

In March 2012, FDA contracted Versar, Inc. to organize and conduct an external peer review of its draft document "Qualitative Risk Assessment: Risk of Activity/Food Combinations for Activities (Outside the Farm Definition) Conducted in a Facility Co-Located on a Farm" (the draft RA). The independent expert peer reviewers (see Section IV below) were selected by Versar, Inc. and also deemed by Versar to have no conflicts of interest. The goal of the peer review was to provide FDA with a comprehensive appraisal of and feedback on the nature of the approach taken, the scope and purpose of the draft RA, the definitions used in the draft RA, the questions asked in the draft RA, and the clarity and transparency of the draft RA. The peer reviewers were first asked to evaluate and comment in a general way about the scientific basis and quality of the draft RA (see "General Impressions" Section III, Part A below). Second, they were asked to respond to a list of specific charge questions that addressed various aspects of the draft RA (see "Peer Reviewer Response to Charge Questions" in Section III, Part B below). Finally, the peer reviewers were asked to provide any additional comments, feedback or

scientific information they had that might improve the draft RA (see “Specific Observations” Section III, Part C).

The draft RA was conducted by FDA to satisfy requirements of the FDA Food Safety Modernization Act (FSMA) for determining whether to exempt small or very small businesses that are engaged only in specific types of on-farm manufacturing, processing, packing, or holding activities that FDA determines to be low risk involving specific foods FDA determines to be low risk from the requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for hazard analysis and risk-based preventive controls and for mandatory inspection frequency, or whether to modify such requirements for such facilities. The RA follows a structured approach, including risk assessment sections on Hazard Identification, Hazard Characterization; Exposure Assessment; and Risk Characterization.

**Charge Question 1.** Are the risk analysis framework and the risk management approach appropriate for the intended purpose of the QRA?

**Charge Question 2.** Are the definitions of “low-risk activity” and “low-risk activity/food combination” reasonable?

**Charge Question 3.** Is the approach for determining food types and activity/food combinations that we considered outside the scope of the draft QRA and those that were included in the draft QRA reasonable given the purpose of the QRA? If not, how might this be revised?

**Charge Question 4.** Are the scope and purpose of the QRA clearly identified? If not, what additional information should be provided?

**Charge Question 5.** Are the questions to be addressed in the QRA appropriate, given the scope and purpose of the QRA? If not, what changes would you suggest?

**Charge Question 6.** Does the QRA adequately cover the activity/food combinations that are not within the farm definition and that would be conducted by farm mixed-type facilities? If not, what other activity/food combinations should be included?

**Charge Question 7.** Considering the scope and purpose of the QRA, are the approaches to hazard identification, hazard characterization, exposure assessment, and risk characterization appropriate?

**Charge Question 8.** Is the report written in a transparent and clear manner? Does the report adequately address the questions and stated objectives? If not, how might the report be revised?

**Charge Question 9.** Do you have any additional comments that might improve the document?

### **III. Peer Reviewer Comments and FDA Response**

Below, we provide the text of each peer reviewer's feedback and responses to the specific charge questions verbatim without attribution to the specific reviewer. FDA considered and used this information to edit, clarify, supplement and improve the draft RA. FDA responded and/or commented in reply to the peer reviewers in instances when doing so was deemed warranted and appropriate but did not respond or comment in all instances.

#### **A. General Impressions**

##### **Reviewer #1**

The FDA report, "DRAFT Qualitative Risk Assessment: Risk of Activity/Food Combinations for Activities (Outside the Farm Definition) Conducted in a Facility Co-Located on a Farm", describes a risk analysis to support decisions for small and very small businesses regarding the need to be registered with FDA or be considered for possible exemptions or exceptions from additional regulatory oversight under FSMA as FDA deems appropriate for low risk activity/food combinations.

The report is well organized and well written for a technical audience. Tables and bulleted lists are used effectively to illustrate the approach and document evidence and decisions. Organizing principles clearly support classification of raw agricultural commodities (RACs) and activities on farms and in food facilities co-located on farms.

The accuracy of information provided is mixed quality. Much of the referenced work is from book chapters and the FDA Bad Bug Book that do not benefit from the full scientific peer review process or an emphasis on risk analysis. As a result, the report does not distinguish between subjective opinions/beliefs of experts and objective scientific findings supported by definitive evidence. The weakness and ambiguity of the evidence for "infective doses" and general principles and guidelines for dose-response assessment for both the likelihood and severity of disease (see Codex Alimentarius Commission 1999, 2011) are not even mentioned in the Hazard Characterization. This weakness impacts the Risk Analysis Framework and the Risk Management Approach, most significantly for Consideration 5. Apparent inconsistencies are noted between FDA summaries (Tables 9 and 10) and results reported in the cited study (Scallan et al. 2011) for *Listeria*, norovirus, and *Salmonella* hospitalization and death rates.

The soundness of conclusions is uncertain due predominantly to weaknesses in the Hazard Characterization. For example, it is unclear if the scientific evidence supports classifying all three pathogens with low frequency of human cases and medium or high rates of hospitalization or death (*C. botulinum*, Hepatitis A virus, *L. monocytogenes*; Table 10, page 43) as having reasonable probability of causing serious adverse health consequences for the RACs considered. In addition, the level of uncertainty and the basis for assumptions are not explicitly addressed.

Additional text acknowledging strengths and limitations of the evidence and describing uncertainty and supporting rationale would improve the report and strengthen the scientific basis of the conclusions.

**Reviewer #2**

The objective of the risk assessment is to identify low risk manufacturing and processing activity/food combinations when conducted on a farm on food other than the farm's own raw agricultural commodities for distribution into commerce. The approach taken is to identify specific types of activities that may occur in a farm environment, what microbial, chemical, and physical hazards are reasonably likely to occur based on commodity and practices, which of these hazards could cause serious adverse health effects, and what inherent food safety controls may exist as part of a given process or practice. Given the Food Safety Modernization Act mandate to conduct a Qualitative Risk Assessment, and the existing risk assessment framework within Codex, this is a reasonable approach to take. The risk analysis was sound and well referenced. The final list of manufacturing and processing activities/food combinations that, when conducted on a farm on food other than the farm's own raw agricultural commodities, present a low risk is reasonable provided the operations are complying with Good Manufacturing Practices.

**Reviewer #3**

Overall, the qualitative risk assessment appears to be fit for the purposes for which it was designed. With the exception of issues noted elsewhere in this review, the report provides a structured, largely transparent and complete characterization of activities which may be given the label "low-risk." The authors have constructed an activity-focused approach which has little formal precedent as compared to the much larger literature that deals with food-hazard combinations. As such, there is little comparable risk assessment literature and few examples to serve as a basis for comparison. In addition, as a novel form of risk assessment, there is an opportunity to think carefully about how the approach is structured and how certain terms may be used (starting with "hazard").

With respect to clarity, the report is somewhat difficult to understand due to the very limited and scattered discussion of the core logic of the risk assessment process. The report would benefit greatly from an overall diagram which describes the inputs, the process and the outcomes in some unified way. The actual judgment being applied in the risk assessment process is buried in a large amount of what is essentially background information (e.g., characterizations of the role of water activity in foods, detailed descriptions of the health effects of particular pathogens that are well known). In addition, the core logic of the risk assessment process (the "risk-based" part) should be described independently of the administrative overlay that relates to the interpretations of definitions of activities that fall in and out of scope of the RA. The risk-based logic should apply equally well to characterize any on-farm activities as being low-risk, regardless of the administrative logic that places activities in and out of scope as a matter of interpreting the statutory definitions of "farm" and other distinctions that are not risk-based, but "rules-based." This might be explained by taking a set of very different activities and explaining the essential logic of the risk assessment process through these examples, including ones that are excluded, included but classified low-risk for various reasons, and included but classified non-low-risk for various reasons. Then, the subsequent detailed characterization of the universe of activities and their inter-relationships with hazards and foods can be detailed without having to explain the risk assessment process along the way.

#### **Reviewer #4**

This qualitative QRA is being generated to respond to the FSMA and on-farm and off-farm operations. Because these were not spelled out in detail in the Act, the FDA is attempting to clarify what would be exempt and what would not. Unfortunately, as is clear from the information presented, this is not obvious and there are many instances where there is a very fine line between exemption or not. The FDA has made a reasonable attempt to help farmers and regulators determine what may constitute risky practices that could lead to a foodborne illness and those that are unlikely to do so. The assessment will not cover every single situation and low risk does not mean no risk. No doubt over time, there will be scenarios that were not apparent to the authors of this assessment, and it will have to be modified as these are documented. Because of the complexity of the different situations the assessment seems rather convoluted and takes careful reading. It is important for the risk managers to understand which farmers who are conducting operations may constitute a moderate to severe risk of causing illness and to find the sections that apply to them. This RA document does not state exactly who this is for and what actions could be taken. It seems to be more of a generic framework from which more specific directions for specific risk managers will be derived. This needs to be made clear in the document. Even in this detailed description of operations, only some examples of potential risk factors for hazard/commodity situations are given. There are undoubtedly many more that may not be apparent to the manager to determine which operations can be assessed to be exempt or not. Also, farmers will need to inform the inspectors if they change any part of their operations that may increase the risk of the products being produced. This means the managers through the inspection system will have to be able to clearly interpret this assessment and explain to the farmers if their operations present anything more than a low risk. To do so will require some training on the inspectors part plus a resource person or persons at more centralized FDA stations to help in giving official advice. This could also fall to third party auditors to carry out. The Conclusions help the farm operations zero into their specific areas but they may still want clarification. Because some terminology may be familiar to some managers and inspections but not all stakeholders applicable to this RA (and many definitions are given throughout the text), a glossary of terms in one place should be included for ease of reference. For instance, one has to infer what RFRs are and why they may be useful.

#### **Reviewer #5**

The draft QRA document provides a detailed and structured approach to the task identified by Congress, as outlined FSMA, determining activity/food combinations that may be considered to be low risk. The information is presented in a logical linear progression from concept and task, to clarification definitions, to risk assessment assumptions and conclusions. Overall the presentation of information is fairly clear (I have noted specific areas below where I think the presentation can be revisited). Some of the content is redundant or found in other documents that can be referenced instead of inserted directly into the text of this output (noted below). The structure of tables (fields included, notation and notes) is sometimes difficult to follow (specifics also noted below). The document successfully provides clear definitions and a framework and in my opinion provides a sound and defensible QRA framework. Based on my knowledge of datasets used (and presented to the reviewers) the information is accurate and I have drawn similar conclusions to those that were presented, based on the information and data sources provided/available. I have detailed some of the shortcomings/limitations of the datasets in the process below and feel that these limitations should be stated or at least addressed in the text of

the document. Ultimately I believe the use of this document will be by regulatory bodies (or the regulated industry) to help define where the activities and food combinations are considered low-risk or not – it would therefore be useful to have the activity/food combinations that were in scope for the QRA and deemed to be not low risk to be acknowledged somewhere in the executive summary (realistically that is where readers will go to look for this information).

## **B. Peer Reviewer Response to Charge Questions**

**Charge Question #1.** Are the risk analysis framework and the risk management approach appropriate for the intended purpose of the QRA?

### **Reviewer #1**

Both the risk analysis framework and the risk management approach may not be appropriate for the intended purpose. It is puzzling that FDA did not cite the two Codex Alimentarius Commission reports on principles and guidelines for microbial risk assessment and risk management (CAC, 1999<sup>1</sup>; CAC 2007<sup>2</sup>). FDA did cite the 2011 update to the 20th volume of the CAC procedural manual, but not fully integrate that work into the risk analysis framework (specifically, regarding magnitude and sources of uncertainties and basis for assumptions).

Regarding Hazard Characterization in the microbial risk assessment process, the first statements in the FDA Hazard Characterization section (page 28) and in CAC Section 4.5 (CAC 1999, page 5 of 6) are consistent, but the second key statement in the same paragraph of the CAC document (“A dose-response assessment should be performed if the data are obtainable.”) was not discussed at all in the report. Dose-dependency of likelihood and severity of disease merits discussion by FDA. Also, additional text is needed in this section to address the strengths and limitations of the “infectious dose” concept and the data or opinions cited.

Regarding the risk management approach (as well as Exposure Assessment), additional clarifying text is needed for Consideration #5 because the frequency and magnitude of exposure are crucial factors influencing likelihood and severity of disease.

### ***FDA Response:***

In revising the risk assessment we have deleted the risk analysis framework section as unnecessary (although we did follow the Codex approach, since it is internationally accepted). Therefore there is no need to refer to the cited Codex documents.

In the document we submitted for external peer review, we had abbreviated “Qualitative Risk Assessment” as “QRA.” However, the abbreviation “QRA” is frequently associated with a quantitative risk assessment. In light of the reviewer’s emphasis on quantitative aspects of a risk assessment (e.g., dose-response), we have shortened our abbreviation to “RA.” We have also revised the document to eliminate the “considerations” in order to streamline the approach in the RA.

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1 Available at [www.codexalimentarius.net/download/standards/357/CXG\\_030e.pdf](http://www.codexalimentarius.net/download/standards/357/CXG_030e.pdf)

2 Available at [www.codexalimentarius.net/download/standards/10741/cxg\\_063e.pdf](http://www.codexalimentarius.net/download/standards/10741/cxg_063e.pdf)

**Reviewer #2**

Yes. Determination of risks based on where the food was packed, handled, manufactured, and/or processed, the type of commodity, and inherent product or process controls is reasonable.

**Reviewer #3**

The framework and approach appear to be a reasonable interpretation of the statutory requirement for a “risk analysis.” From this standpoint of attempting to review a risk assessment, the approach seems to unnecessarily conflate the estimation of the risk associated with an activity, with a diverse range of risk management issues, legal interpretations and other material that, while important to the risk management process, seems to be unnecessary to the discussion of the essential question of the level of risk associated with an activity. Ideally, there would be more separation between the risk estimation process and the risk management overlay on the estimation process. This would certainly support the ability of the risk estimation process to be understood and to be re-applied in a generic sense (as suggested in the summary. page 66). The generic properties of the risk assessment process are essentially buried in a certain amount of extraneous text that makes it difficult to conclude that there is generic utility to the process described.

***FDA Response:***

We revised the draft RA to move an extensive regulatory background to an Appendix. We also revised the risk characterization section of the document to first present the risk characterization of activity/food combinations without the overlay of the applicable statutory and regulatory framework. Doing so focuses the risk characterization on the risk of the activity/food combinations themselves. In Appendix 2, we add that regulatory overlay and characterize the risk of activity/food combinations in groups shaped by the applicable regulatory factors and the resulting activity classifications.

**Reviewer #4**

As indicated above, this is a qualitative risk assessment and definitions of terms are unique to this assessment. How low is low risk, etc? As long as the managers understand and accept these, it should be OK. However, as indicated above in the General Impressions, change is inevitable as the managing process gets underway. So, there should be flexibility to make modifications. However, in a regulatory field, making frequent changes is not desirable. A pilot is desirable to test out the system. This may have been done but I could see no reference to one.

**Reviewer #5**

Yes, these approaches are very appropriate for the intended purpose of this QRA. The systematic evaluation of activities, foods, hazards and probabilities is the best evidenced-based process to answer this question. The risk analysis framework also allows for a transparent process to show impacted parties how the decisions were arrived at.

**Charge Question #2.** Are the definitions of “low-risk activity” and “low-risk activity/food combination” reasonable?

**Reviewer #1**

The terms are useful as defined. However, the definitions could also present the specific criteria for “reasonably likely” and “reasonable probability” here, or refer to the Risk Characterization section (pages 42-43) where criteria are applied.

***FDA response:***

We have updated the definitions to improve readability.

**Reviewer #2**

The definitions are made reasonable and clear by referencing Codex criteria for assessing risks.

**Reviewer #3**

The definitions of low-risk activity etc. are given in a number of places in different ways. There are qualitative definitions, and then later in the document, there is a set of scoring rules that ultimately define the actual implementation of the definition (combinations of “lows, mediums, highs” etc. that determine the fate of the activity as “low-risk”). This actual definition should be provided up-front in the report, since this definition essentially frames the entire discussion of what evidence is required to make the ultimate judgment of “low-risk.”

***FDA Response:***

We revised the discussion of the definitions of low-risk activity and low-risk activity/food combination to improve readability. We also provided more explanation about how we ordered information related to frequency and severity of illnesses, and about how we then grouped the rates of illness, hospitalization, and death into “high,” “medium” and “low” categories. The definitions appear earlier in the RA now that several sections, including the extensive regulatory background have been moved.

**Reviewer #4**

See under #1.

**Reviewer #5**

The content within each definition is suitable. The wording is not clear (mainly because of the sentence structure). I would suggest:

We are defining “low-risk activity” to mean an activity that is not reasonably likely to introduce a hazard, for which there is a reasonable probability that handling or consumption of the food, will cause serious adverse health consequences or death to humans and, the activity does not significantly minimize or prevent the hazard.

And:

We are defining “low-risk activity/food combination” to mean a low-risk activity that applies to a specific food (i.e., the activity is not reasonably likely to introduce a hazard, for which there is a reasonable probability that handling or consumption of the food, will cause serious adverse health consequences or death to humans and, the activity does not significantly minimize or prevent the hazard in the specified food).

***FDA Response:***

We revised the discussion of the definitions of low-risk activity and low-risk activity/food combination to improve readability.

**Charge Question #3.** Is the approach for determining food types and activity/food combinations that we considered outside the scope of the draft QRA and those that were included in the draft QRA reasonable given the purpose of the QRA? If not, how might this be revised?

**Reviewer #1**

The approach for inclusion and exclusion of food types and activity/food combinations seems reasonable.

**Reviewer #2**

Excluding certain food types and activity/food combinations was reasonable given that these are covered by other regulations or will be regulated as farm activities covered within the produce safety standards under FSMA.

**Reviewer #3**

The approach to defining the scope of the RA appears to be reasonable, but is largely “rules-based” and therefore could be done outside of the RA document. Since the concept of risk is not employed in making these scope decisions, the RA should simply refer to another document which applies these rules-based interpretations. In addition, the language of the RA could be dramatically simplified by using short forms like “Type 1” or “Type 2” activities which have been precisely defined early in the document. Repeated use of phrases like “Certain manufacturing and processing activities that might be conducted on a farm on types of food other than the farm’s own RAC” make reading the document extremely tedious, as compared to referring to “Type 2 activities.”

***FDA Response:***

We revised the draft RA to move an extensive regulatory background to an Appendix. We also revised the risk characterization section of the document to first present the risk characterization of activity/food combinations without the overlay of the applicable statutory and regulatory framework. Doing so focuses the risk characterization on the risk of the activity/food combinations themselves. In Appendix 2, we add that regulatory overlay and characterize the risk of activity/food combinations in groups shaped by the applicable regulatory factors and the resulting activity classifications. We provided simple names for each group (e.g., Regulatory Group Type 1, etc.)

**Reviewer #4**

I would say reasonable for the present combinations but likely to be added to or modified once the program gets underway. So, some degree of flexibility is necessary.

**Reviewer #5**

One difficulty throughout the evaluation of this document is that reviewers were not provided with some oft-cited and important task orders (most importantly being the Muth, 2011 report which forms the basis for many of the definition decisions and consumption). Especially the

citation of ‘Food Sector Study classifies 175 small and very small facilities co-located on farms that produce “Food Preparations, Not Elsewhere Classified.”’ Since there is likely such diversity and niche markets/products/activities having access to that document, or having a summary presented as an appendix, would have led to a more concise review. In the absence of this document, a summary of the findings in the Muth, 2011 report as an appendix would be useful.

One specific definition as part of the cutting/coring/chopping/shredding/slicing/peeling/trimming activity, which definitely relates to this QRA is around the existient [sic] definition of cut leafy greens (as defined here:

<http://www.fda.gov/Food/FoodSafety/RetailFoodProtection/ucm218750.htm> - which links directly to the time/temperature control for safety foods as defined in the risk management approach).

The term “leafy greens” does not include herbs such as cilantro or parsley. Lettuce and other leafy greens cut from their root in the field with no other processing are considered raw agricultural commodities (RACs) and are not included in the definition of “cut leafy greens” and are therefore not considered a PHF/TCS Food, as defined and applied in the 2009 Food Code.

There are multiple ways to harvest leafy greens destined to be consumed raw where the cut zone at harvest is not the root zone (head leafy greens). The above definition, and the harvest exclusions discussed in Table 3, provide somewhat of a grey area. It is currently unclear in this document and in other FDA guidance referred to in this document as to whether a non-root zone cut in the field, of a leafy green (own RAC) would be an activity that would be considered cut or not (as cut from their root is the key term). I’d suggest clarifying this here.

***FDA Response:***

The report by Muth et al. will be in the docket for the proposed rule to establish regulations implementing section 418 of the FD&C Act. The RA does not apply to activities (such as harvesting) solely within the farm definition.

**Charge Question #4.** Are the scope and purpose of the QRA clearly identified? If not, what additional information should be provided?

**Reviewer #1**

The scope and purpose are well defined in the context of the regulatory decisions of interest. What is unclear is the intended audience for the report. If the report is intended for the public or small and very small businesses, additional text may be needed.

***FDA Response:***

We have added text clarifying that the report is intended for risk managers at FDA to consider in determining, in part, whether to establish any exemptions from, or modifications to, requirements that would otherwise apply to small or very small farm mixed-type facilities.

**Reviewer #2**

The discussion clearly explained that the FSMA directed FDA to conduct this QRA.

**Reviewer #3**

The scope and purpose are certainly identified, but should be more clearly justified or amended. The exclusion of some foods because they require continuous refrigeration and therefore cannot be “low risk” seems odd, since the risk assessment itself would have come to the same conclusion, with greater transparency and consistency, as compared to a reasonable but somewhat arbitrary exclusion. The arbitrariness stems from the fact that other foods could have been summarily excluded for different but equally reasonable reasons, but were included in the risk assessment.

***FDA Response:***

We both revised the discussion of foods that were out of scope and distinguished the criteria for these foods being “out of scope foods” from the criteria for low-risk activity and low-risk activity/food combination.

**Reviewer #4**

I do not believe that imported farm products are included but the reference to coffee and cocoa may indicate that to readers. It should clearly state the scope of the RA to the 50 US states.

Lines 1229-1234. the low proportion of farms relative to sales may give a global US perspective, but with certain communities it may be much higher, particularly rural areas and market towns.

***FDA Response:***

We added a specific statement clarifying that the RA applies to activities conducted on foods by small and very small farm mixed-type facilities, including both domestic and foreign facilities.

**Reviewer #5**

Yes, for the most part. Some specifics are contained in the line descriptions below.

**Charge Question #5:** Are the questions to be addressed in the QRA appropriate, given the scope and purpose of the QRA? If not, what changes would you suggest?

**Reviewer #1**

The nine questions are appropriate to frame the QRA for the present scope and purpose.

**Reviewer #2**

The questions are appropriate and provide a pathway for the reader to follow the sequence of steps that FDA took to complete the QRA.

**Reviewer #3**

The questions are a natural progression, but would be improved by adding an additional up-front question: What are the key criteria and steps in the decision logic employed in the risk assessment that operationalize the qualitative definition of “low-risk.”

***FDA Response:***

We made a series of revisions to improve readability and to simplify the presentation of the results.

**Reviewer #4**

Yes, reasonable but probably not complete; only after putting the RA into practice will other points and questions emerge.

**Reviewer #5**

A question that would be useful, between question 7 and 8 would be “which of these activities have been demonstrated to be carried out poorly in the past” and weight heavier in the QRA calculations. For example, while 7 addresses the possibility for pathogens to be introduced in cutting, what is missing in the question list is information on the likelihood of the activity being carried out poorly (cross-contamination, poor cleaning and sanitizing) enhancing the likelihood of introduction. Likewise could be the in process of baking, cooking. Are heat treatments carried out properly (with correct measures). While I’m not sure the data exists, efforts should be made to seek it out from the literature and provide assumptions here if not found.

**FDA Response:**

We do not include a question on whether certain activities such as cross-contamination, poor cleaning and sanitizing are carried out poorly, as these are addressed through GMPs and the RA was done in part to help assess whether controls beyond GMPs would be needed. With respect to activities such as heat treatments, these would be preventive controls and activity/food combinations involving these treatments are generally not considered low risk.

**Charge Question #6.** Does the QRA adequately cover the activity/food combinations that are not within the farm definition and that would be conducted by farm mixed-type facilities? If not, what other activity/food combinations should be included?

**Reviewer #1**

Food/activity combinations adequately cover the farm mixed-type facilities.

**Reviewer #2**

The activity/food combinations appear to be complete at this time. See answer to question 9 for related comment.

**Reviewer #3**

I lack sufficient knowledge of the details of on-farm food processing to address this question.

**Reviewer #4**

Because *Cyclospora* has been associated with RTE fruits or vegetables like berries and garnishes, e.g. basil, since the 1990s, it should be included as a pathogen. See below for the latest FoodNet data. I do see that *Cryptosporidium* has higher numbers of cases (but not as high as *Giardia*), but the foodborne link must be hard to estimate for *Cryptosporidium* and *Giardia*. It is hard to find from Scallan et al how these large foodborne illness cases numbers for parasites come from, but outbreaks from *Cyclospora* appear about once a year.

Rebecca L. Hall, Jeffrey L. Jones, Sharon Hurd, Glenda Smith, Barbara E. Mahon, and Barbara L. Herwaldt. 2012. Population-based active surveillance for *Cyclospora* infection—United

States, Foodborne Diseases Active Surveillance Network (FoodNet), 1997–2009. 10.may.12.Clin Infect Dis. (2012) 54 (suppl 5): S411-S417.  
[http://cid.oxfordjournals.org/content/54/suppl\\_5/S411.abstract](http://cid.oxfordjournals.org/content/54/suppl_5/S411.abstract)

**Abstract:**

*Background.* Cyclosporiasis is an enteric disease caused by the parasite *Cyclospora cayetanensis*. Since the mid-1990s, the Centers for Disease Control and Prevention has been notified of cases through various reporting and surveillance mechanisms.

*Methods.* We summarized data regarding laboratory-confirmed cases of *Cyclospora* infection reported during 1997–2009 via the Foodborne Diseases Active Surveillance Network (FoodNet), which gradually expanded to include 10 sites (Connecticut, Georgia, Maryland, Minnesota, New Mexico, Oregon, Tennessee, and selected counties in California, Colorado, and New York) that represent approximately 15% of the US population. Since 2004, the number of sites has remained constant and data on the international travel history and outbreak status of cases have been collected.

*Results.* A total of 370 cases were reported, 70.3% (260) of which were in residents of Connecticut (134 [36.2%]) and Georgia (126 [34.1%]), which on average during this 13-year period accounted for 29.0% of the total FoodNet population under surveillance. Positive stool specimens were collected in all months of the year, with a peak in June and July (208 cases [56.2%]). Approximately half (48.6%) of the 185 cases reported during 2004–2009 were associated with international travel, known outbreaks, or both.

*Conclusions.* The reported cases were concentrated in time (spring and summer) and place (2 of 10 sites). The extent to which the geographic concentration reflects higher rates of testing, more sensitive testing methods, or higher exposure/infection rates is unknown. Clinicians should include *Cyclospora* infection in the differential diagnosis of prolonged or relapsing diarrheal illness and explicitly request stool examinations for this parasite.

Here are other combinations that may or may not have been considered:

*E. coli* in walnuts (14 cases in Canada); *Salmonella* in pistachios, Brazil nuts (also aflatoxin in Brazil nuts).

*E. coli* in cookie dough (flour).

What about tahini from sesame seeds in small operations (*Salmonella*), may not apply to the USA?

Here are two pathogens that we need to be on the lookout, whether now or possibly in the future, as they have been either found in farm environments (*C. dif*) or at least one foodborne outbreak (MRSA): *Clostridium difficile* and methicillin resistant *Staphylococcus aureus*

Gould LH and Limbago B. *Clostridium difficile* in Food and Domestic Animals: A New Foodborne Pathogen? 2010. *Clinical Infectious Diseases* 51:577–582.

Gould and Limbago, of the Centers for Disease Control and Prevention (CDC), acknowledge that *Clostridium difficile* infection is increasingly recognized as a cause of diarrhea in outpatients and individuals lacking contact with a healthcare facility, and now, it may be transmitted via food in the community setting. Their research has been published in the September 2010 issue of [Clinical Infectious Diseases](#). They note, "Food has been hypothesized as a possible source of *C. difficile* in community settings, but evidence to confirm or refute this hypothesis is incomplete. *C. difficile* is recognized as both a gut colonizer and cause of diarrhea in food animals. Recent studies have isolated *C. difficile* from retail foods intended for human consumption in the United States, Canada, and Europe and from meat products intended for consumption by pets. These findings support concerns about foodborne acquisition of this pathogen through consumption or handling of contaminated products; however, no published studies have documented consumption of any food product as a risk factor for CDI. An improved understanding of the relationship between animal and human strains of *C. difficile* will help to evaluate the potential for foodborne transmission and the role of animal-human contacts in *C. difficile* epidemiology." In their study, Gould and Limbago summarize the available data on *C. difficile* in animals and food and discuss data gaps that must be addressed to clarify whether foodborne transmission of this pathogen might occur, and if so, whether this route might be important in the epidemiology of CDI.

The researchers point out, "Data on the presence and prevalence of *C. difficile* in food products are newly available, and there are limited epidemiologic data to connect *C. difficile* found in the food supply to human illness. However, the epidemiology of *C. difficile* infection is changing, including an increase in both incidence and severity of disease, emergence of a new epidemic strain (ribotype 027/NAP1), and an apparent increase in infections among persons in community settings. Increasing rates of CDI in the community have raised questions about origins of new human strains, sources of human *C. difficile* acquisition, and risk factors for the development of infection. In addition to causing human disease, CDI is recognized as a cause of epidemic disease in piglets, and *C. difficile* is also commonly found in other food animals, including cattle and chickens. Some of the *C. difficile* strains most commonly identified in food animals appear to be emerging as causes of disease in humans, especially among humans with community-associated CDI. Although a link between *C. difficile* carriage in animals and disease in humans has not been adequately defined, some investigators have suggested that food animals may play an important role in the expansion of pathogenic *C. difficile* clones and in transmission to humans through food."

Gould and Limbago continue, "If transmission indeed occurs from animals to humans, it will be essential to characterize the dynamics of this transmission, including whether transmission occurs through direct animal-to-human contact or through indirect means, such as consumption of contaminated foods. Increasingly, foods such as produce have been recognized as vehicles for pathogen transmission in outbreaks. In many of these outbreaks, a contaminated environment (eg, soil or irrigation water) appears to be responsible for delivery of bacteria to the food plants. In some instances, pathogens are internalized by the plant during growth, limiting the efficacy of control measures based on sanitation or washing. *C. difficile* has also been isolated from produce and can be recovered from a wide variety of environmental sources, including soil, sea water, and fresh water. Thus, it is possible that humans and animals are frequently exposed to *C.*

difficile spores from multiple sources. Whether, when, and how frequently this exposure leads to disease is a critical question for improved control of CDI."

Gould and Limbago emphasize that a number of questions must be answered to determine whether foodborne transmission of *C. difficile* occurs and to determine the possible impact of low-level spore contamination on the safety of the food supply: "For example, the infectious dose of *C. difficile* for humans is unknown; if the infectious dose were known, it could be compared with the microbial burden that is typically present on contaminated foods at the point of consumption. Infectious dose is likely to vary depending on host factors, including age, underlying medical conditions, and exposure to antibiotics and acid - reducing medications, and these factors are likely to be very different between hospitalized and community populations. *C. difficile* is not considered to be part of the normal human intestinal flora, but limited studies have demonstrated presence of toxigenic *C. difficile* in 3 percent to 5 percent of asymptomatic persons in the community. It is unknown whether this finding represents subclinical infection, colonization, or transient pass-through of ingested spores. It is also unknown whether or how often *C. difficile* is transmitted from animals to humans, or vice versa, or whether presence of common strains in animals and humans reflects exposure to a common environmental reservoir. Surveillance for human and animal infections is needed and should include subtyping studies designed to distinguish between common sources of animal and human infection or animal - to - human transmission. Detailed strain typing and epidemiologic investigations designed to evaluate the role of foodborne transmission during *C. difficile* outbreaks might help to determine whether *C. difficile* strains found in humans are linked to the food supply. Additionally, studies are needed to characterize food and environmental exposures in persons with community-associated CDI who do not have any health care exposures and to clarify whether implicated risk factors also impact transmission in healthcare settings."

The researchers add that additional studies are needed to develop consensus best-practice methods to test meats and other foods for *C. difficile*, as well as to understand surface decontamination on *C. difficile* spores in and on meat and other food products and, if foodborne transmission proves to be a mechanism, to evaluate other possible approaches to limit transmission by this route. They note, "It is reasonable to assume that the general public is and has been often exposed to low numbers of potentially infectious *C. difficile* spores. There is currently limited epidemiologic evidence to support or refute the hypothesis that *C. difficile* is transmitted by the foodborne route; the presence of *C. difficile* on retail foods suggests but does not prove that some proportion of infections is acquired this way. The food supply may thus serve as a source of new strains causing human infections; alternatively, food could be another constant and normally innocuous exposure. It is very clear that more research is needed to better understand the dynamics of and risk factors for development of CDI among persons in the community, including the relevance and possible importance of foodborne transmission."

Scott R. Curry, Jane W. Marsh, Jessica L. Schlackman and Lee H. Harrison. 2012. Prevalence of *Clostridium difficile* in uncooked ground meat products from Pittsburgh, Pennsylvania. 24.may.12.*Appl. Environ. Microbiol.* June 2012 vol. 78 no. 12 4183-4186.  
<http://aem.asm.org/content/78/12/4183.abstract?etoc>

**Abstract:**

The prevalence of *Clostridium difficile* in retail meat samples has varied widely. The food supply may be a source for *C. difficile* infections. A total of 102 ground meat and sausage samples from 3 grocers in Pittsburgh, PA, were cultured for *C. difficile*. Brand A pork sausages were resampled between May 2011 and January 2012. Two out of 102 (2.0%) meat products initially sampled were positive for *C. difficile*; both were pork sausage from brand A from the same processing facility (facility A). On subsequent sampling of brand A products, 10/19 samples from processing facility A and 1/10 samples from 3 other facilities were positive for *C. difficile*. The isolates recovered were inferred ribotype 078, comprising 6 genotypes. The prevalence of *C. difficile* in retail meat may not be as high as previously reported in North America. When contamination occurs, it may be related to events at processing facilities.

There are also new Canadian studies; there may be strain differences between disease strains in hospitals and those found in manure, but increasingly it is thought that the agricultural environment may bring into the hospital some of these acquired strains.

B. Crago, C. Ferrato, S.J. Drews, L.W. Svenson, G. Tyrrell, M. Louie. 2012. Prevalence of *Staphylococcus aureus* and Methicillin-resistant *Staphylococcus aureus* (MRSA) in food samples associated with foodborne illness in Alberta, Canada from 2007 to 2010. 09.may.12.*Food Microbiology*.

<http://www.sciencedirect.com/science/article/pii/S0740002012000949>

**Abstract:**

Consumption of foods containing *Staphylococcus aureus* can cause severe gastro-intestinal illness. Given the fact that over the past decade, Canada has seen increasing rates of methicillin-resistant *S. aureus* (MRSA) carriage and infection, the objective of this study was to investigate the impact of methicillin-susceptible *S. aureus* (MSSA) and MRSA on foodborne illness in Alberta, Canada. Between January 2007 and December 2010, there were 693 food samples associated with foodborne investigations submitted to the Alberta Provincial Laboratory for Public Health (ProvLab). These foods were screened for: *Bacillus cereus*, *Clostridium perfringens*, *Staphylococcus aureus*, *Aeromonas* spp., *Campylobacter* spp., *Escherichia coli* O157:H7, *Salmonella*, *Shigella* spp., and *Yersinia* spp. *S. aureus* was identified in 10.5% (73/693) of samples, and of these, 59% (43/73) were co-contaminated with at least one other organism on the screening panel. The *S. aureus* positive samples included 29 meat, 20 prepared foods containing meat, 11 prepared foods not containing meat, 10 dairy, and three produce. Methicillin-resistance was not detected in any isolates tested. These findings indicate that the presence of *S. aureus* in food associated with foodborne investigations is a cause for concern, and although MRSA was not found, the potential for outbreaks exists, and ongoing surveillance should be sustained.

**Highlights:**

- The presence of *S. aureus* found in food a cause for concern in Alberta.
- Identification of *S. aureus* was most commonly associated with protein-rich foods.
- Although MRSA was not found it is important to continue monitoring.

FoodNet, RFRs, and food recalls only cover certain agent food combinations.

There are frequent observations and even complaints of illness about mold growth in jams, jellies and maple sirup. These occur when there is long term storage at room temperatures with air access. Consumers may choose to skim these off. This may apply more to farmers' markets. Certainly low risk if CDC data the main source used.

### **Chemical hazards**

Lines 298-299. In the text one criterion is determining the risk from a single serving vs. long-term exposure. From the conference call discussion it would appear that a short term exposure through an agent causing acute effects are deemed at a higher risk. This is not explained in the text and in fact could be questioned; long term exposure on through farm use to some chemicals could reduce life expectancy though not easily measurable). Lines 529-537 indicate that the hazards are based on CDC surveillance data based on outbreak investigations. These are slanted towards biological agents that produce acute effects. I notice that low = No more than 50,000 illnesses, impossible to determine for chemical or physical hazards. I think some effort should try and bring in those agents that would cause serious chronic effects. If not, it should be clearly stated that these are excluded for the present from this RA even though some agents may have an impact on HALYs. I agree, for instance, that pesticide residues are low in the surveys done, but these probably do not cover small farm operations with limited fruit and vegetable distribution. It is not so much the spraying of pesticides that are the major risk factor for this group of chemicals (except for the farmer) but the accidental or inappropriate use of a variety of farm chemicals because of lack of labels, poor storage, or a careless employee (e.g., dioxins from heating fuel). Not easy to monitor, however. Although not so frequent today, small operations still may use copper piping for soft drinks (also heavy metals for equipment, containers and storage). These have caused illnesses in the past. I think there should be a brief rationale given for choosing this criterion and how it is weighted.

### **Physical hazards**

Lines 966-980. Physical hazards may be limited in their action to cause severe illnesses, but they are the ones that cause a large number of complaints and law suits because the stone, bone fragment, glass, metal shavings, etc., is immediately available to the complainant. Also, small farms will not have the resources to check over their products for these physical hazards to the same extent as larger operations.

### ***FDA Response:***

This RA is not intended to be a comprehensive review of the relevant literature. Thus, while some of these references would be relevant, they would not impact the results of the RA. We reviewed the information graciously provided by the reviewer. We note that *Cyclospora* is a hazard related to growing fruits and vegetables, which is outside the scope of the RA. We did not feel it necessary that the RA address every pathogen (or outbreak) associated with every product, but rather selected representative pathogens for food types. Thus, *Salmonella* in tree nuts and grains is adequate to address *E. coli* in walnuts or flour, respectively, with respect to whether an activity/food combination is low risk. We did not address pathogens such as *C. difficile* or MRSA because we cannot at this time say they present a reasonable probability of adverse health consequences or death.

### **Reviewer #5**

Yes, although one difficulty throughout the evaluation of this document, especially around activities is that reviewers were not provided with some oft-cited and important task orders (most importantly being the Muth, 2011 report which forms the basis for many of the definition decisions and consumption). Especially the 'Food Sector Study classifies 175 small and very small facilities co-located on farms that produce "Food Preparations, Not Elsewhere Classified."' Since there is likely such diversity and niche markets/products/activities having access to that document, or having a summary presented as an appendix, would have led to a more concise review.

I understand (from Table 1) that trimming is a harvest activity (and why it is not included in Table 14 and is in Table 16) but I think for clarification the activity either requires it's own row, or conversely can be dropped from Table 16 as when it is not conducted at harvest, trimming is not possible (and it becomes a cut).

### ***FDA Response:***

The report by Muth et al. will be in the docket for the proposed rule to establish regulations implementing section 418 of the FD&C Act. The RA does not apply to activities (such as harvesting) solely within the farm definition.

**Charge Question #7.** Considering the scope and purpose of the QRA, are the approaches to hazard identification, hazard characterization, exposure assessment, and risk characterization appropriate?

### **Reviewer #1**

The approaches presented for hazard identification, hazard characterization, and risk characterization may be inappropriate and are inconsistent with the 6-page CAC report (1999; Principles and Guidelines for the Conduct of Microbiological Risk Assessment)<sup>3</sup>, as well with other microbial risk assessment reports and manuscripts in the published literature. The report could be improved with additional attention to both the scientific basis of the assessment and its structure. Suggestions for improvement include the following:

The Hazard Identification section could include discussion of all three aspects of the disease triangle (host, pathogen, environment) and interactions resulting in adverse health effects, as well as the disease surveillance data that FDA presented. For example, disease descriptions cited from the Bad Bug Book and books in the Hazard Characterization section are more appropriate in this section.

The Hazard Characterization section should include discussion of general principles and guidelines for dose-response assessment, as well as available data and published models of dose-response relationships for the pathogens of interest. The lack of acknowledgement by FDA that such data exist is puzzling, particularly when other groups at CFSAN have prepared dose-response assessments. The authors of this report may be reluctant to address the complex nature of dose-response relationships, with so many ambiguous and/or conflicting datasets (e.g., non-typhoidal salmonellosis, listeriosis) subject to various driving factors of the disease triangle and

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3 Available at [www.codexalimentarius.net/download/standards/357/CXG\\_030e.pdf](http://www.codexalimentarius.net/download/standards/357/CXG_030e.pdf)

their interactions that confound both experimental and observational data. However, opinions about the infectious dose, without uncertainty bounds, are subjective, and citing them as scientific facts or reliable evidence for predicting human disease is problematic, misleading at best.

Studies typically cited as evidence of the “infective dose” are typically outbreak investigations. Rarely are high quality data generated for definitive estimation of ingested doses (with uncertainty bounds) from suspect foods that caused (and did not cause) infection and illness in populations exposed. When outbreak investigations measure pathogen counts in companion samples of suspect foods and estimate quantity of suspect food consumed, the known heterogeneity of distribution of pathogens in foods still suggests high uncertainty for the estimates, even though the estimates might be reported as definitive ingested or infectious doses.

The CAC principles and guidelines document describes Risk Characterization as an integration of outputs from hazard identification, exposure assessment, and hazard characterization. The characterization of the hazards according to Consideration #5 (page 42-43) seems to be based solely on the hazard identification section (epidemiologic frequencies of disease and rates of hospitalization and death for unknown ingested doses that are not directly attributable to specific foods). Additional text is needed in this section as an overview describing how the evidence (or expert opinion) is ‘mapped’ to activity/food categories to generate risk rankings. Although the authors define symbols for their risk matrix tables (X as for low-risk and O as NOT low-risk or reasonable probability of serious illness or death given exposure), the criteria for assigning X or O (and reasonable probability) are unclear. Though the authors cite derivation of risk rankings from Considerations #1, #2, and #3, the sources of evidence for making these assignments across food and activity combinations are unclear.

#### ***FDA Response:***

We believe that the approaches presented for Hazard Identification, Hazard Characterization, and Risk Characterization are generally consistent with the CAC *Principles and Guidelines for the Conduct of Microbiological Risk Assessment*. However, we extensively revised the Exposure Assessment and Risk Characterization sections to improve readability and transparency and to ensure it is consistent (to the extent possible) with the Codex *Principles and Guidelines for the Conduct of Microbiological Risk Assessment* as applicable to a qualitative risk assessment.

The purpose of the Hazard Identification is to identify the microorganisms or toxins of concern for the food. While we do not disagree that the disease descriptions in the Hazard Characterization section could be included here, the CAC Guidelines indicate that Hazard Characterization provides a description of the severity and duration of adverse effects, so we have retained this information in that section. We have added a sentence in Hazard Identification that states, “Whether or not a hazard can cause adverse health effects in an individual depends on the host, the agent and the environment.” However, we do not believe that further discussion of this is needed to meet the purpose of this RA.

We disagree that a discussion of general principles and guidelines for dose-response assessment is needed in this RA. Since we did not consider it practical to assess the risk of all pathogen/food

combinations (due in part to data limitations and because we did not feel it necessary to achieve the purpose of this RA), we do not do a dose response assessment for each pathogen that could pose a hazard in foods. We note in our data limitations section that we lack data to conduct a dose-response assessment for hazard characterization for foods that may be manufactured, processed, packed or held by small and very small farm mixed-type facilities. We do, however, consider frequency and level of contamination in the exposure assessment section and note that for some pathogens only a few organisms can cause infection. We note that the risk of illness from foodborne pathogens that cause illness from consumption of only a few cells significantly increases if growth occurs and that conditions that allow growth increases the risk for illness. Thus, we approach infectious dose in a very general way and focus primarily on the outcome - the nature, severity, and duration of adverse effects that may result from ingestion of the hazard.

The tables have been revised and the criteria for assigning a “yes” or “no” (rather than an “X” or “O”) to an activity/food combination have been clarified.

## **Reviewer #2**

These are appropriate approaches since they are consistent with Codex standards.

## **Reviewer #3**

*Hazard Identification:* This report’s unique focus on activities presents an opportunity to expand the use of the definition of hazard. The Codex definition of hazard is broader than is often employed and includes references to “conditions.” The essential purposes of this type of risk assessment (which will become increasingly required under FSMA) might be greatly served by exploiting this expanded concept of hazard, rather than relying on the purely biological definition of hazard. This is common in other industries where the primary concern is the failure of various protective mechanisms or organizational failures, rather than identifying [sic] chemical or biological properties as the hazards. An inappropriate or absent allergen label, or practices that do not adequately prevent cross-contamination of allergens are examples of “failures” or “conditions” that might be included by employing the expanded definition of hazard.

For greater transparency, since the risk assessment process essentially sets aside a considerable portion of the overall set of potentially relevant hazards (most chemicals, radioactive hazards, physical hazards), this should be better explained as a major conclusion in itself, with a correspondingly detailed justification (preferably, early in the document and all in one place).

*Hazard Characterization:* The report presents a variety of background material on hazards that are essentially boilerplate or “cut-and-paste” discussions of the health effect of various pathogens. The report should focus on how this report uniquely characterizes the hazards (severity of disease and frequency in the population) and simply cite other sources of information for evidence that is not truly part of this risk assessment activity.

*Exposure Assessment:* Similarly to the Hazard Characterization, the report presents a variety of background material on properties related to microbial growth. The report should focus on how this report uniquely characterizes exposure. The concept of exposure is uniquely related to the definition of hazard, such that opportunities to expand the concept of hazard would also allow for a similar expansion to the concept of hazard (e.g., the frequency with which a package is not

labeled properly would be an estimate of exposure to an “informational” hazard, if such a hazard was defined by adopting the broader possibilities for definitions).

The exposure assessment, while technically included, appears to be essentially unused in the overall analysis. It may be included out of a sense of obligation to a four-step process, rather than having an actual role in the risk assessment except to argue for the exclusion of certain hazards. The exposure assessment should be summarized and its role in the risk estimation process made clear. If it not directly used, much of the current exposure assessment text could be deleted.

***FDA Response:***

We enhanced the discussion within the Exposure Assessment section, in part by moving some discussion from the Risk Characterization section to the discussion in the Exposure Assessment section.

**Reviewer #4**

As a general principle, yes.

**Reviewer #5**

There are limitations in the data used in Part III Hazard Identification (beginning on line 508). The text currently lacks information on how decisions were made to select CDC data on outbreak and illnesses from 2003-2007 as the only source of identification data. This is particularly curious as the source for this information also included data from 2008 (why not use that as well?). The data source is fine (and likely would not change the outputs), but a justification as to why not to go back historically beyond 2003 is definitely needed.

Public funds-generated data that should be available (I’m making an assumption here) that could have made the QRA more robust is active surveillance data generated through the USDA ARS MDP program as well as state sampling programs. It seems as though probability of hazard assumptions could have been reduced and created a more concrete data foundation for conclusions to be drawn from. While I’m not sure the output would have been much different, I agree with the statements about presence on lines 1012-1020 (which are in a somewhat different context) and that absence can be a function of methods and other factors; the data does exist and should at least be referenced as to why it was not accessed/included.

A further omission I think would have been useful for the project team to address (even if it is just to say why it was not included) is *Toxoplasma gondii*. Because of the large public health burden, this pathogen should be noted as to why it was not included. As an aside, from anecdotal evidence of feline pest control as well as the potential for polyculture farms (those that produce livestock, produce and the types of products included within the scope of this document) at facilities defined as mixed-type could increase the presence of the pathogen in these sites (although probability-supporting data likely does not exist).

***FDA Response:***

We used the most current data available, as these are more likely to represent the current situation with respect to illnesses and their sources. Data from the MDP program are related to raw agricultural commodities and are most relevant to on-farm production, which is outside the

scope of the RA. Although we did not use the MDP data, the hazards associated with fruits and vegetables as determined by MDP testing are addressed in this RA and thus the data would not have impacted the conclusions of this RA. We did not address pathogens such as *Toxoplasma gondii* because we cannot at this time say it presents a reasonable probability of adverse health consequences or death for the foods within scope of the RA.

**Charge Question #8.** Is the report written in a transparent and clear manner? Does the report adequately address the questions and stated objectives? If not, how might the report be revised?

**Reviewer #1**

Although the report is well-written and the text is generally clear, the transparency of the report needs improvement. For example, though the approach is clearly presented for considering various “infectious doses” estimated from outbreaks, the text is not transparent on the limitations of the data and assumptions that form the basis of these estimates. A transparent report would acknowledge the limitations and uncertainties rather than present estimates without error bounds that could be misinterpreted by readers as scientifically irrefutable facts. Uncertainty bounds including both measurement and sampling errors are needed to judge the quality of the estimates for extrapolation to other conditions and other populations as in this report.

Improvements in transparency are also needed to address other sources of data (and uncertainty) for Hazard Characterization: human and animal clinical studies. Even if FDA chooses not to apply dose-response data and models available for many of the pathogens of concerns for this qualitative assessment, the report at least should acknowledge the data available and the ambiguity of the evidence for predicting doses that will cause severe human illness because disease severity is dependent on pathogen dose, as well as host and environmental factors.

**FDA Response:**

We added a section directed to data limitations and note uncertainty within the text.

**Reviewer #2**

The report is difficult to wade through initially. However, after careful reading, the intent and logical pathway to answering the questions at the end of the report become clear. The literature review on hazard characterization is thorough and very helpful. I have no recommendations for revising the report.

**FDA Response:**

We revised the draft RA to move an extensive regulatory background to an Appendix. We believe that doing so improves the readability of the early sections of the draft RA, while retaining the necessary regulatory background within the document.

**Reviewer #3**

The report certainly has elements of transparency, but ultimately is not very clear.

An overall diagram which describes the flow of evidence and various decision points in reaching a “low-risk” determination in the process would be extremely helpful to provide a framework for understanding the report.

As discussed in other comments, the report would greatly benefit from a clear description of this specific risk estimation process, with separation from the administrative overlays that determine the scope of activities, and reduced discussion of generic information that is not newly processed in this risk assessment (e.g., generic descriptions of listeriosis, and the role of water activity). The purpose of the report is not educational, and the reader should be expected to be generally familiar with these concepts or should be referred to reference material for generic background.

***FDA Response:***

We revised the draft RA to move an extensive regulatory background to an Appendix. We also revised the risk characterization section of the document to first present the risk characterization of activity/food combinations without the overlay of the applicable statutory and regulatory framework. Doing so focuses the risk characterization on the risk of the activity/food combinations themselves. In Appendix 2, we add that regulatory overlay and characterize the risk of activity/food combinations in groups shaped by the applicable regulatory factors and the resulting activity classifications.

We retained general descriptions of topics such as listeriosis and water activity because these descriptions provide context (e.g., about the severity of illness from consumption of food contaminated with pathogens and about the scientific basis for how a property of a food can affect the potential for growth of pathogens). These aspects are important in characterizing the risk from the foods in scope of the RA.

**Reviewer #4**

As indicated in the general comments, it is hard for the reader not familiar with the legal restraints and FDA infrastructure and terminology including risk assessment terms to follow this RA. Therefore, it depends on the audience being addressed. Eventually, there is a farmer-inspector interaction that will determine which operations are exempt and which not. Maybe, a less complicated document can be prepared for the farmer to understand with this one as a background reference, and can be supplemented through personal contact and webinars.

***FDA Response:***

We added a statement clarifying that risk managers at FDA will consider the results of the risk analysis presented in the RA in determining, in part, whether to establish any exemptions from, or modifications to, requirements that would otherwise apply to small or very small farm mixed-type facilities. Farmers and inspectors will refer to the final regulation, rather than the RA, to determine whether an exemption applies to a particular facility.

**Reviewer #5**

With my comments addressed above (Muth report availability, decisions for inclusion and exclusion of hazards, more information on assumptions) the report is written in a transparent and clear manner. A further step to add to this is to include links to the FDA task order reports that were referenced that are not available online (and if they are currently available, linking directly to them to aid in searching them out).

***FDA Response:***

The report by Muth et al. will be in the docket for the proposed rule to establish regulations implementing section 418 of the FD&C Act.

**Charge Question #9.** Do you have any additional comments that might improve the document?

**Reviewer #1**

Though this review focused on FDA's treatment of microbial hazards, the FDA presented concise and well-targeted analysis of chemical, physical, and radiological hazards of potential concern.

**Reviewer #2**

Perhaps it is not within the scope of this document, but there should be a mechanism in place to periodically review the conclusions of this document. Over time, it may become apparent that currently un-identified activities/food combinations may be more appropriately designated as low risk. Alternatively, future recalls, outbreaks, or microbial survey data might show that a previously identified low risk activities/food combination should be moved to a higher risk category. It might also be useful to include a statement that these activities/food combinations are considered low risk as long as Good Manufacturing Practices (21CFR Part 110) are followed.

***FDA Response:***

We will use the RA, in part, to determine whether exemptions from regulations implementing section 418 of the FD&C Act are warranted for small and very small farm mixed-type facilities. We would review the conclusions of the RA if new data or information raise a question about such exemptions.

**Reviewer #3**

None.

**Reviewer #4**

1) How are certain specialty operations managed where farm products are sold to the public in artisanal or religious communities, like the Amish? Though many of these will be on-site sales, others may market their products further afield including across state borders. Also, when is an operation considered a farm and when is it home preparation for stands and farmers' markets? If these are covered elsewhere, they should at least be mentioned.

***FDA Response:***

These questions relate to risk management and regulatory policy and thus are outside the scope of the RA, but may be covered in future regulations and/or guidance documents

2) Note the new Washington State Cottage Food Act and rules that may have to be considered when this RA is to be implemented. Some of the same foods are being addressed. Text below.

WASHINGTON: New Cottage Food rules available for review, comment

09.may.12

Washington State Department of Agriculture

<http://agr.wa.gov/News/2012/12-10.aspx>

OLYMPIA -- Jelly producers across the state applauded last year when the Legislature adopted the Cottage Food Act. The law legalizes the sale of low-risk foods made in the home, allowing potentially hundreds of new small businesses into farmers markets and other direct-sales venues.

Up to this point, all foods intended for sale to the public were produced in licensed commercial kitchens. This requirement was seen as a barrier to some small businesses, especially in rural areas where commercial kitchens were not available for rent.

Since the law was passed, 250 home-based businesses have expressed interest in applying for a Cottage Foods license. The Washington State Department of Agriculture (WSDA) estimates that more than 1,000 Washington businesses may eventually apply for the license. Oregon, which enacted a similar law, has around 800 licensed cottage food operations.

“The interest in this new license has been astounding,” said WSDA’s Kirk Robinson, assistant director for food safety and consumer services. “Working with our applicants, we’ve developed a common-sense approach in helping these new home-based food businesses open their doors, while protecting the public from food-borne illness. We’re excited about working with these new operations.”

WSDA spent several months meeting with interested bakers and others to write the rule necessary to implement the law. The draft rule, now available for review, stipulates which foods may be produced, the required licenses and inspections, as well as labeling requirements.

Products allowed for sale under the draft rule include: breads, cakes, cookies, granola, nuts, jams and jellies, and other low-risk products. All recipes should have a cook step to prevent the spread of food-borne illness or be made from shelf-stable ingredients.

Prohibited products include: meat jerkies, poultry, seafood, canned or processed fruits and vegetables, fresh juices, pickles, dairy products and other higher-risk foods.

Under the law, gross sales of cottage food products may not exceed \$15,000 per year. Only direct sales to consumers are allowed; mail order or internet sales are not permitted.

Cottage food operations will be inspected annually by WSDA. Operators must have a food worker card from the local health department, a requirement typical for restaurant workers. Homes not on a public water supply must test their water for bacterial contamination. Costs to the business to meet all requirements should range from \$230 to \$290 per year.

Operations must implement acceptable sanitary standards. Food contact surfaces and floors must be smooth and easily cleanable. Pets and children under 6 must be excluded from the kitchen when food is being prepared.

Written comments on the draft rule can be submitted to [jcarlson@agr.wa.gov](mailto:jcarlson@agr.wa.gov). WSDA will conduct a public hearing at 1 p.m. on May 22 in Room 172, Natural Resources Building, 1111 Washington St. SE, Olympia.

**FDA Response:**

We considered similar products in the RA, where they were in scope, and appreciate receiving this information. The RA was conducted for FDA risk managers to determine whether certain facilities should be exempt from requirements or whether requirements should be modified with respect to Federal regulations for hazard analysis and risk-based preventive controls; we recognize that state regulatory agencies may have their own determinations with respect to risk of foods that are within the scope of this RA.

3) The text does not have a complete or most recent lit review. Many are taken from the text book of Doyle et al., 2007. The following are examples of what could be added.

L.A. Kuntz. Food Product Design, 2012. Keeping food safety in the mix: food safety in grain-based and bakery products.

H.V. Smith, S.M. Caccio, N. Cook, R.A.B. Nichols, A. Tait. 2007. Cryptosporidium and Giardia as foodborne zoonoses *Veterinary Parasitology* 149: 29–40.

J. E. Matthews, B. W. Dickey, R. D. Miller, J. R. Felzer, B. P. Dawson, A. S. Lee, J. J. Rocks, J. Kiel, J. S. Montes, C. L. Moe, J. N. S. Eisenberg and J. S. Leon. 2012. The epidemiology of published norovirus outbreaks: a review of risk factors associated with attack rate and genogroup. *Epidemiology and Infection* 140:1161-1172.

Rebecca L. Hall, Jeffrey L. Jones, Sharon Hurd, Glenda Smith, Barbara E. Mahon, and Barbara L. Herwaldt. 2012. Population-based active surveillance for Cyclospora infection—United States, Foodborne Diseases Active Surveillance Network (FoodNet), 1997–2009. *Clin Infect Dis.* 54 (suppl 5): S411-S417.

**FDA Response:**

Information from text books is useful because it compiles data from the literature. This RA is not intended to contain a comprehensive review of the relevant literature. Thus, while some of these references would be relevant, we do not believe they are needed to accomplish the purpose of the RA.

4) For tables citing refs, prefer two or more confirmatory refs, especially if one is a text book.

5) Lines 1232-1234. "Thus, on a relative basis, the overall exposure of the population to all foods produced at farm mixed-type facilities is low and the exposure to such foods containing hazards would be even lower." Yes, the population is low but the risk for individuals.

**FDA Response:**

Information from text books is useful because it compiles data from the literature. In most instances, additional citations could have been provided, but we do not believe they are needed for the purpose of the RA.

We acknowledge in the RA that the risk of foodborne illness can be addressed on a per serving basis (i.e., the amount of food consumed by an individual on a single eating occasion) or on a per

annum basis (i.e., the amount of food consumed by a specified population over the course of a year). We believe that activity/food combinations identified as low risk in the RA present a low risk for individuals as well as for the population in general.

#### 6) Comments on the tables

Table 10: are *Cryptosporidium* and *E. coli* really that equal in Table 10. Outbreaks for *E. coli* outweigh those for Crypto, at least in the public's mind. Severity for the at-risk population is also higher for *E. coli*. Most large Crypto outbreaks involve water; probably small family ones do not get investigated to source.

#### **FDA Response:**

We displayed the findings based on the objective measures of the rates of hospitalization and death. We added tables demonstrating how we qualitatively characterized risk as “high,” “medium” or “low” in order to determine whether hazards present a reasonable probability of causing serious adverse health consequences or death.

Table 11: Foreign objects Low Single eating occasion Low No Is a broken tooth from a stone or a cut throat/gut from glass low?

#### **FDA Response:**

“Low risk” does not mean “no risk.” Our experience with foreign objects in food is that they generally do not present a reasonable probability of causing serious adverse health consequences or death. This was supported by data from the Reportable Food Registry.

Table 12: "some fruits like berries cannot be washed or heated"

Washing fruits and vegetables with water contaminated with *Cryptosporidium*. Use of contaminated water in a food that does not receive a treatment that will remove or inactivate the organism.

Table 12: What happened to aflatoxin in Table 12; it is missing?

#### **FDA Response:**

The purpose of the RA was in part to determine the need for preventive controls required by section 418 of the FD&C Act for small and very small farm mixed-type facilities in light of the regulatory framework that would apply to such facilities that would become exempt from, or subject to modified requirements for, the requirements for hazard analysis and risk-based preventive controls that would be established under section 418 of the FD&C Act. The regulatory framework that would apply to such facilities includes the current good manufacturing practice (CGMP) requirements in 21 CFR part 110 for manufacturing, packing, or holding human food and the adulteration provisions of section 402 of the FD&C Act. Under the CGMPs, the facility would be required to address the safety of water that comes in contact with the food.

Mycotoxins such as aflatoxin were determined to not pose a reasonable probability of causing serious adverse health consequences or death, and thus were not addressed in Table 12.

Table 13: "Fruits/vegetables Packing/Re-Packing (including conveying and weighing incidental to packing/repacking)" How about food handler contamination of berries during sorting and packing.

***FDA Response:***

The purpose of the RA was in part to determine the need for preventive controls required by section 418 of the FD&C Act for small and very small farm mixed-type facilities in light of the regulatory framework that would apply to such facilities that would become exempt from, or subject to modified requirements for, the requirements for hazard analysis and risk-based preventive controls that would be established under section 418 of the FD&C Act. The regulatory framework that would apply to such facilities includes the current good manufacturing practice (CGMP) requirements in 21 CFR part 110 for manufacturing, packing, or holding human food and the adulteration provisions of section 402 of the FD&C Act. Under the CGMPs, the facility would be required to address personal hygiene of food handlers.

Table 13: Fruits and vegetables Storing (Ambient cold, or controlled atmosphere) What about Listeria in stored field cabbage which led to an outbreak in 1981?

***FDA Response:***

The outbreak of listeriosis that resulted from Listeria in stored field cabbage can be attributed to fertilization of the cabbage with sheep manure; this is related to growing and harvesting, which is outside the scope of the RA.

Table 14: What about seeds/oils?

***FDA Response:***

Oil from seeds was identified in the RA as having inherent controls for hazards reasonably likely to occur.

Table 14: Improper drying can led to mold growth in several commodities.

***FDA Response:***

Mycotoxins such as aflatoxin were determined to not pose a reasonable probability of causing serious adverse health consequences or death. Moreover, the regulatory framework that would apply to facilities producing such commodities includes the adulteration provisions of section 402 of the FD&C Act.

Table 14: Metal or other physical risks may be present through grinding.

***FDA Response:***

Physical hazards were determined to not pose a reasonable probability of causing serious adverse health consequences or death.

Table 14: "Jams/jellies" Inappropriate preparation and storage may result in mold growth (lines 959-960).

***FDA Response:***

Growth of mold does not pose a reasonable probability of causing serious adverse health consequences or death.

Table 15: Any outbreaks from coffee beans (possible aflatoxin presence) since it is listed [sic] as a food of concern?

Table 15: "Jams/jellies" Mold may enter if the vacuum seal is not complete.

***FDA Response:***

We did not find any outbreaks of illness due to coffee beans. Growth of mold does not pose a reasonable probability of causing serious adverse health consequences or death.

Table 15: Excessive amounts of several additives have led to illnesses like nitrates and MSG.

Table 15: Heavy metals as present in processing equipment or containers should be at least discussed.

***FDA Response:***

There are many potential hazards that could be discussed. We do not believe these issues pose a reasonable probability of causing serious adverse health consequences or death.

Table 16a: "Treating against pests other than during growing, e.g. fumigation". But may be against the law for residues to be present.

***FDA Response:***

The focus of this RA is on the risk presented by activity/food combinations. Legal issues such as this are outside the scope of the RA.

Table 16B: Typo - "Grinding/Milling/Cracking/Ccrushing)" Also, Metal particles could be present.

***FDA Response:***

Typographical errors have been corrected in the revised RA.

Table 17: "The activity is reasonably likely to introduce, or create the potential for, a hazard by spreading biological hazards such as *E. coli* O157 and *Salmonella* that may be present on the exterior of the fruit or vegetable". These can come from soil, manure, especially if the farm has animals present.

Table 17: "pathogens that survive cooking, e.g., *C. botulinum*, which under." What does which under mean, maybe look up somewhere else for *C. bot*?

***FDA Response:***

We did not discuss the source of pathogens on the exterior of fruits and vegetables, but agree that soil and manure are likely sources.

The partial clause at the end of the sentence (“which under”) was a typographical error. We corrected the error.

**Reviewer #5**

I understand the need for clarifying the history of the document and where it fits into the current regulatory structure as introduced in section, I. BACKGROUND AND PURPOSE, A. Statutory and Regulatory Framework, but wading through the most confusing information over the first four content pages (lines 1-123) could possibly be condensed and the full text included as an appendix.

There are inconsistencies between the use of ‘low risk’ and ‘low-risk’

There should be some sort of guidance within the document on where a shared use kitchen facility on a farm would fall (and if it was any different if a business operated on the farm site that was not owned by the farmer).

***FDA Response:***

We moved the detailed discussion of the legal and regulatory framework to an Appendix. We addressed the inconsistencies between the use of “low risk” and “low-risk.” We continue to use “low-risk” when that term is used as an adjective (e.g., low-risk activity/food combination” and otherwise use “low risk” (e.g., in Question 9 - “Which activity/food combinations are low risk?”).

The issue of a shared use kitchen facility on a farm is a regulatory policy issue and thus is outside the scope of the RA, but may be covered in future guidance documents.

## C. Specific Observations

**Table 1: Specific Observations by Reviewer #1**

Page	Line	Comment	FDA Response
7-10	Table 3	Clarity of the table could be improved. Suggest the following: decrease width of first column and increase width of last column; use smaller font or narrower spacing between rows of text; merge cells in the first column with the same classification; insert new row within columns 2 and 3 with centered subheadings (“Discussion” in first row and “Examples” in second row for each classification) rather than italicized terms in each cell of these two columns.	We moved Table 3 (which was largely directed to regulatory issues) to an Appendix but did not otherwise change it. Some of the suggestions for improved display would interfere with guidelines for making documents accessible to persons using assistive technology.
43	Table 10	The comment column could be merged for all hazards and listed only once for cleaner presentation.	“Table 10” is now “Table 14.” We included the information in a footnote to the table rather than in a column.

**Table 2: Specific Observations by Reviewer #2**

Page	Line	Comment	FDA Response
68	Reference #13	The referenced web site at ( <a href="http://www.cdc.gov/ncidod/dvrd/revb/gastro/norovirus-factsheet.htm">http://www.cdc.gov/ncidod/dvrd/revb/gastro/norovirus-factsheet.htm</a> ) is redirected to <a href="http://www.cdc.gov/norovirus/hcp/index.html">http://www.cdc.gov/norovirus/hcp/index.html</a> .	We updated the reference to an April 2012 version of CDC’s Web site.
68	Reference #19, 20, and 21	Links lead to error messages.	The error messages derived from format features inadvertently introduced by software for managing references. We are correcting these to the extent practical.
69	Reference #26-38	Should be updated to refer to recently updated 2012 2nd edition of the Bad Bug Book at <a href="http://www.fda.gov/food/foodsafety/foodborneillness/foodborneillnessfoodbornepathogensnaturaltoxins/badbugbook/default.htm">http://www.fda.gov/food/foodsafety/foodborneillness/foodborneillnessfoodbornepathogensnaturaltoxins/badbugbook/default.htm</a> .	We replaced all references to specific chapters of the Bad Bug Book with a reference to the 2012 complete Bad Bug Book.

**Table 3: Specific Observations by Reviewer #3**

Page	Line	Comment
None provided.		

**Table 4: Specific Observations by Reviewer #4**

Page	Line	Comment
None provided.		

**Table 5: Specific Observations by Reviewer #5**

Page	Line	Comment	FDA Response
2	54	“Low-risk” There should be a sentence that explains that this term was not defined in FSMA (it takes another 250 lines to get to the definition).	With the removal of the regulatory text to an Appendix, the definition appears early in the RA.
6	159	Table 2 is confusing; I'm not clear on why this is a table, what it is trying to relay.  Also need to clarify the wording in the organizing principle to have a common start. ('basic', and then 3 'activities should'). It would be  I'm also not clear why 5 (for consumption on the farm) is needed at all (and throughout the document)? Could this not be taken care of in scoping by saying this is only for commercial products?	We moved the applicable discussion to an Appendix where it is more clearly directed to regulatory matters rather than to the scientific risk assessment.
6	161-162	I do have a problem with this definition when it comes to rented land. A common example would be a tomato farmer who produces and packs on his/her own land – as well as contracting with another landowner for the use of their fields. The producer is responsible for managing this rented land but would not fall under the own RACs definition above and would move from out of scope to not low risk based on the QRA. Even though the ownership of the product and management practices would be carried out by the same person/system. This needs to be addressed for consistency.	This regulatory issue is outside the scope of the RA.

<b>Page</b>	<b>Line</b>	<b>Comment</b>	<b>FDA Response</b>
7-10		<p>Table 3 – Discussion is messy, I think this whole table's orientation should be changed to landscape.</p> <p>Harvesting definition needs to be clarified: “Harvesting does not include activities that change a RAC into processed food” either reference to the below rows on manufacture or processing – or a definition found in another guidance document/regulation.</p> <p>What would be really useful are 2 or 3 flow charts showing what Table 3 is trying to represent stepping a product from harvest to manufacture/processing.</p>	<p>Certain design features on FDA’s Web site prevent us from using landscape orientation when we intend to make a document available on our Web site.</p> <p>A more detailed discussion of the definitions in Table 3 will be available in an upcoming rulemaking that would establish those definitions. The abbreviated discussion in the RA is intended only to provide context that the classification of an activity as manufacturing, processing, packing, or holding depends on several factors.</p>
11	201-218	Should go earlier into the background and purpose.	We moved most of the information that had been in the introduction to an appendix and the discussion that had been on lines 201-218 is now very early in the document.
12	234-236	This clarification around handling practices warrants a couple more sentences to clarify what these specific handling practices would be.	We expanded the discussion as suggested.
12	235	Is the first time the words "public health" appear public health risk needs to be defined earlier - along with risk analysis framework – in background/purpose.	We do not believe a definition of public health risk is necessary. The term appears once in the revised risk assessment, and it would be easily understood in the context given.

Page	Line	Comment	FDA Response
12	243	A table that summarizes the controls that may be needed would be useful here (and referenced to other documents) – even a footnote would be useful.	The key document that could be referenced will be the upcoming proposed rule to implement section 418 of the FD&C Act
12	261	This has already been said above (lines 227-231) cut from above.	We deleted the re-statement that had been on line 261.
29	683-684	Also common is the relative rate at which the hazard is found in the food supply – see my note in answer to charge question 7.	We lack data on the “rate” at which a hazard is found in the food supply.
29	685	Should be hospitalizations or, better yet, hospitalization rate (since that is what is argued a few sentences later).	We revised to emphasize the rate of hospitalization and death as a measure of severity.
29	690-694	Wording is awkward – revisit to clarify (I’m not entirely sure exactly what the point is here).	To add clarity, we added tables ordering the information related to frequency and severity to group into “high,” “medium” and “low” categories.
29-30	705-732	The information is not as technical or heavily referenced as the paragraphs from lines 734-812. I prefer the later as it demonstrates a better evidence base. It really just reads inconsistently.	Since the RA is not intended to provide a comprehensive review of the literature, additional references are not needed for <i>B. cereus</i> and <i>C. botulinum</i> .
30	730	Botulism intoxication (not poisoning).	We revised to botulism intoxication.
30	748	Infectious dose as a term is incorrect - should be median infectious dose. The infectious dose could be as small as 1.	We used the term used in the cited reference.
36-40	1009-1156	This section misses information on actions/activities that impact frequency of contamination and solely focuses on growth post-contamination. These introduction activities should be noted here in this section.	We describe activities that could introduce, or increase the potential for, a hazard in a table.

Page	Line	Comment	FDA Response
41	1232 - 1234	This statement about low and even lower is correct if surveillance data showed that these facilities had the same rate of initial contamination. I'm not sure that exists - and if it does, it wasn't included here.	We have no data to suggest that the foods from farm mixed-type facilities present a higher or lower rate of contamination than other foods.
43	1289	Table 10 column on comments isn't needed - can be included as a note at the bottom.	We moved the information to a footnote and deleted the column.
46	1375	Table 12 is a bit confusing – comments are sometimes references, sometimes actual notes. The subdivision within the examples of interventions is also awkward. This could be split into multiple tables or some sort of a flow-chart/figure	We split the information into several tables.
49	1417	Instead of x and o, can low risk and not low risk be used?	We revised to communicate “low risk” and “not low risk” using “Yes” and “No,” respectively.

#### IV. External Peer Reviewers

##### **Benjamin Chapman, Ph.D.**

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Dr. Chapman is an assistant professor and food safety extension specialist in the Department of 4-H Youth Development and Family & Consumer Sciences at North Carolina State University. He provides leadership and technical expertise for North Carolina’s statewide Extension food safety education program and develops and evaluates education programs that focus on safe food handling from farm-to-fork.

##### **Margaret E. (Peg) Coleman, MS**

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Ms. Coleman is a medical microbiologist/risk analyst and is the sole proprietor of Coleman Scientific Consulting. She is a risk assessor with thirty years experience in regulatory, consulting, and research environments synthesizing bodies of scientific data and technical information to support risk assessments for chemical, physical, and microbial hazards in air, food, and water. She has served as an expert reviewer on projects with National Academies of

Science committees, multiple US government agencies, and the European Food Safety Authority to develop comprehensive, defensible guidance for conducting risk assessment from inhalation, dermal, and oral exposures to chemical and microbial hazards and to improve scientific support and risk analysis practice in support of robust analytic-deliberative processes that effectively communicate about risks and interventions. She is a leader in advancing development of empirical and mechanistic models for more robust microbial risk analysis essential for effective exercise of cycles of analysis and deliberation in preparedness planning for natural and intentional contamination events.

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Dr. LaBorde is an Associate Professor and Extension Specialist, Department of Food Science, The Pennsylvania State University, University Park, PA. He specializes in research on quality improvement and microbial safety of fresh and processed fruits and vegetables and in extension services for the development of food safety programs for fruit, vegetable, and mushroom growers, packers, and processors.

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Mr. Paoli is a Principal Risk Scientist and Chief Operating Officer of Risk Sciences International, Inc. He has experience in diverse risk domains, including microbiological, toxicological, and nutritional hazards; climate change impact assessment; air and water quality; medical and engineering devices; risks to cultural and museum collections; socio-economic risk assessment; and risk-based priority-setting across multiple hazards. He oversees operations of a professional services consulting firm, provides project management for a broad array of projects in public sector risk management as applied to public and environmental protection, provides policy and strategic advice (primarily to public sector clients in the application of risk management and risk assessment), and provides quantitative analytical services on selected projects. He has served as an expert panel member for the National Academy of Sciences, Canadian National Roundtable on the Environment and the Economy, and the Food and Agriculture Organization/World Health Organization.

**Ewen Cameron David Todd, Ph.D.**

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Dr. Todd is recognized internationally for his work on foodborne disease and its surveillance and costs, developing microbial risk assessments, the impact of seafood toxins on disease, and

detection of pathogens in foods. He has developed methods to detect pathogens, such as *E. coli* O157 and *Salmonella*. He has been active in developing and preparing microbial risk assessments in collaboration with mathematical modelers. For instance, he headed a team from Health Canada and the Canadian Food Inspection Agency to produce a risk assessment for *Salmonella* Enteritidis in shell eggs in Canada. He has conducted other risk assessments including two on *Listeria monocytogenes* in chopped cabbage and *E. coli* O157:H7 in shredded lettuce.